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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,431	12/05/2005	Anne Fournillier	034548-001	1577

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
07/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/559,431	FOURNILLIER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-40* is/are pending in the application.

4a) Of the above claim(s) *18-20,30,31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29,32 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on April 24, 2008 has been acknowledged. Claims 21, 29, 32, 34 have been amended. New claims 38-40 have been added. Claims 1-17 have been canceled. Claims 18-40 are pending. Claims 18-20, 30-31, 33 and 35 were withdrawn from consideration. Claims 21-23, 26-29, 32, 34 and 36-40 in the scope of poxvirus vector are considered before the examiner.

Foreign Priority

1. Acknowledgment has been made to the foreign priority documents submitted on April 24, 2008 by applicants timely.

2.

Withdrawn Claim Rejections - 35 USC § 112 6th paragraph

3. The rejection of Claims 21 and 34 under 35 U.S.C. 112, six paragraph has been withdrawn necessitate by Applicants' amendment.

4.

Withdrawn Claim Rejections - 35 USC § 112 1st paragraph

5. The rejection of Claims 29 and 37 under 35 U.S.C. 112, first paragraph, has been removed necessitated by Applicants' amendment.

6.

Withdrawn Claim Rejections - 35 USC § 102

7. The rejection of claims 21, 23, 26, 28, 29, 35, 36 under 35 U.S.C. 102(b) as being anticipated by Panchi et al. (J. Virol. Jan 2003, Vol. 77, No. 1, pp. 382-390) has been removed necessitated by Applicants' amendment, which limits the peptide consisting of NS3/4 and NS5b rather than the entire sequence of NS5 (NS5 includes NS5a and NS5b).

8. The rejection of claims 21, 23, 26, 28, 29, 35 under 35 U.S.C. 102(e) as being anticipated by US patent 6,986,892 B1 to Coil et al. has been removed necessitated by Applicants' amendment, which limits the peptide consisting of NS3/4 and NS5b rather than the entire sequence of NS5 (NS5 includes NS5a and NS5b).

9. The rejection of claims 21, 23, 28 and 36 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US patent NO.

6,312,889A to Houghton et al. in light of the disclosure by Clark B. (J. Gene. Virol. 1997, Vol. 78, pp. 2397-2410) has been removed in light of Applicants' amendment and persuasive argument.

10.

Claim Rejections - 35 USC § 102/103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 21-23, 26-29, 32-34, 36-40 are still rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/30812A2 to Palliard et al. or US Patent No. 7,285,539B2 to Palliard or US Patent No. 6,562,346B1 to Palliard et al.

14. Applicants argue that all references by Palliard et al. rely on HCV NS3, NS4, and NS5a or alternatively HCV NS3, NS4, NS5a and NS5b expressed as a single chain polypeptide (fused together as in the HCV genome) or as individual polypeptides. The presence of NS5a is essential to Pallliard's compositions, vectors and methods, particularly as two epitopes were identified in NS5a that activate the HCV-specific T cell response *(see* page 15, lines 22-25 of W001/30812;

column 10, lines 35-40 of US 6,562,346; and column 10, lines 41-49 of US 7,285,539). Applicants emphasize that these epitopes are present respectively at positions 2152-2160 (HEYPVGSOL; SEO ID NO: 1) and at positions 2224-2238 (AELIEANLLWRQEMG; SEQ ID NO: 2) within NS5a. Therefore, a person of ordinary skill in the art would have expected that NS5a was necessary to provide effective anti-HCV immunity. Accordingly, the skilled person would not have been motivated to exclude NS5a, as in the present expression vectors, and would not have had a reasonable expectation of success.

15. Applicants' argument has been respectfully considered; however, it is not found persuasive for the following reasons: Palliard et al. in example 11, explicitly teaches an expression plasmid vector that expresses a polynucleotide encoding NS3NS4 and NS5b (NS345b), which is used for priming the immune response against HCV followed by a boost immunization with another plasmid encoding NS5a (See example 11 taught by all cited patents). In this case, the NS3, NS4 and NS5b are expressed together rather than by individual plasmid. Because none of the claimed expression vector and the expression vector cited in the references by Palliard et al. is described as a bicistronic vector, they are considered to be a structurally same expression vectors with the regulatory elements placed at the 5' of the coding sequences of NS3, NS4 and NS5, the plasmid DNA and the method of using the plasmid DNA encoding the NS345b meet the limitations of claims 21, 23, 28 and 29, although epitopes at positions 2152-2160 (HEYPVGSOL; SEO ID NO: 1) and 2224-2238 are located in NS5a.

16. Palliard et al. also teach in all cited references that the polynucleotide sequences encoding the NS3, NS4 andNS5b can be derived from either same or different HCV serotypes, and the method for using said plasmid vector is to induce a T cell immune response, wherein the administration of the plasmid into a host indicates the host cells have been transformed in vivo to expressed the non-structural protein antigen s of NS345b. They also tech that vaccinia viral vector can be used for delivering the HCV immunogenic polynucleotide. Therefore, claims 21-23, 26-28, 38 and 39 are still anticipated by the cited references.

17. Or alternative, for claims 29, 32, 34, 36-37, 39 and 40, it would have been obviously for a person ordinarily skilled in the art to construct the DAN expression vectors expressing a polynucleotide encoding HCV NS3, NS4 and NS5b antigen polypeptides from either same or different genotype by one plasmid or more than one plasmids, because all NS3, NS4 and NS5b

have been approved to be immunogenic when they are used as DNA for immunization individually or in a combination. Therefore, it is also obvious for any ordinary skilled in the art to place the expression vector or vectors in a kit for a convenience of utilization.

18. Hence, absence any unexpected result, the rejection is still maintained.

19. Upon further considered the pending claims, new Grounds of Rejections are made set forth below:

Claim Rejections - 35 USC § 101

20. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

21. Claim 28 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Because there is no recitation of isolation or synthesis in front of the claimed compound, the claimed compound read on transgene animal including human, which are considered to be non-patentable subject matter within the scope of 35 U.S.C. 101. See Official Gazett, 1077 O.G. April 21, 1987. It is recommended that the claim incorporates the claim language, "isolated" to overcome this rejection.

22.

Claim Rejections - 35 USC § 112

23. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claims 32 and 34 are rejected 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a DNA molecule encoding HCV antigenic polyprotein or polypeptide to induce an immune response, does not reasonably provide enablement for using said DNA molecule as a vaccine to prevent HCV infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

25. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following: 1). Nature of the invention, 2). State of art, 3). unpredictability of the field, 4). Scope of the claims, 5). Working example and guidance taught in the specification, 6). Level of skill in the art 7). Amount of the work to fulfill the scope of the invention.

26. The nature of the invention is directed to a DNA construct encoding a HCV polyprotein antigen comprising NS3, NS4 and NS5, and the administration of said DNA molecule in mice induce both cellular and humoral immune responses. However, the scope of the claims read on using said composition to prevent an HCV infection.

27. State of art teach that development of HCV vaccine has been studied with several HCV encoded antigen protein including the, non-structural protein NS3mn, NS4, and NS5 and combination thereof. Both cellular and humoral immune response has been detected. However, none of these vaccine compositions have been approved to be successfully for preventing the HCV infection. The development of HCV vaccine is extremely unpredictable because the following problems: (1). The asymptomatic or inconsistent of HCV infection make it hard to assess any effective remedy in the clinic, (2). High heterogenecity of the HCV genotype prevent one genotype of HCV vaccine can be used for the protection other genotypes of HCV or even the same virus isolation, (3). Neutralizing antibody response to HCV has been difficulty to assess, (4). A relative week immune response to the HCV antigen, and (5). The safety concerns about HCV vaccine, especially the 5' region of the NS3 gene has been tested to be tumorogenic in nude mice and in tissue culture cells. Therefore, in order to prove the efficacy of the HCV vaccine, a large primate, such as chimpanzees rather than a small animal models, are required (See detail discussions by Hsu et al. Clinics in Liver disease 1999, Vol. 3, pp. 901-915 and Dr. Robert Purcell, Hepatology 1997, Vol. 26, pp. 11S-14S).

28. The specification of the present applicant only present that DNA molecule is constructed to comprise HCV NS3, NS4, NSa5 and NS5b.Adminstering a composition comprising the plasmid DNA molecule(s) is able to induce both cellular and humoral immune responses in mice. However, there is no working examples or guidance that injection of any or all HCV DNA composition can prevent an HCV infection.

29. The invention involves one of the most complex and unpredictable fields of developing HCV vaccine. Therefore, the level of the skill in art is very high. Significant hurdles remain to be overcome in order for the skilled artisan to make and use successfully the HCV DNA as a vaccine. Applicants are reminded that a limited in vitro experimental result cannot be extrapolated into a result from an in vivo setting experiment.

30. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

31. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

32. Claim 38 and 39 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-11 of copending Application No. 11,723,638. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the rejected claims and the claims in co-pending Application have overlapping scopes.

33. In the instant case, the rejected claims are more generic and broadly directed to a method using a polynucleotide encoding NS3, NS4 and NS5b with a generic expression vector as one of three choices for inducing cellular immune response, whereas the conflict claims in the copending Application is more specifically directed to a method using a polynucleotide encoding HCV NS3, NS4 and NS5b as only one approach for inducing T cell-mediated immune response. Therefore, the pending claims cite all limitations required by claims 38 and 39. Although they are not cited identically, they have overlapping scopes, and are not patentably distinct each from other.

34. An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887,225 USPQ 645 (fed. Cir. 1985).

35. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

36.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/
Primary Examiner, Art Unit 1648